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10/589,469	08/14/2006	Gianfranco Merizzi	52290	7234

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EXAMINER	
ZAREK, PAUL E	
ART UNIT	PAPER NUMBER
1617	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,469	MERIZZI, GIANFRANCO	
	Examiner	Art Unit	
	Paul Zarek	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 August 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/14/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 5-10 have been amended by the Applicant in correspondence filed on 08/14/2006. Claims 1-10 are currently pending. This is the first Office Action on the merits of the claim(s).

Priority

2. Applicant's claim for the benefit of a prior-filed international application PCT/EP05/01818 (filed on 02/22/2005) under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 02/22/2005.

3. Acknowledgment is made of applicant's claim for foreign priority to Italian application T02004A000124 (filed on 03/01/2004) under 35 U.S.C. 119(a)-(d). The foreign priority date of the instant application is 03/01/2004.

Claim Rejections - 35 USC § 112 (2nd paragraph)

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-8 provides for the use of a compound of formula (I), (II), or (III), but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. For

art purposes, Claims 1-4 are construed to be a method of making formula (I), (II), or (III). Claims 5 and 6 are interpreted to be methods of treating the diseases listed in the claims.

7. Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 6 recites the limitation "[U]se of a compound as identified in Claim 1 for the treatment selected from the pathologies . . ." in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Claim 1 specifies the use of the claimed compound for neurodegenerative diseases only. There is no mention of pathologies related to diseases/disorders that are not neurodegenerative in origin, such as ischemia/reperfusion of the heart, diabetes, cancer, etc.

8. Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948);

and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 8 recites the broad recitation "quantities of from 0.01 to 200 mg/kg of body weight," and the claim also recites "preferably from 0.5 to 20 mg/kg of body weight" which is the narrower statement of the range/limitation.

Claim Rejections - 35 USC § 112 (1st paragraph)

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Claims 1-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for Parkinson's disease and ischemia/reperfusion injury, does not reasonably provide enablement for treating a disease or pathology not associated with Parkinson's disease or ischemia/reperfusion, or prevention of any disease or pathology. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

11. *In re Wands*, 858 F.2d at 736-40, 8 USPQ2d at 1403-07, set forth eight factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." (MPEP § 2164.01(a))

a. *The breadth of the claim*: Claims 1-8 are drawn to the use of a formula (I), (II), or (III) for the treatment or prophylaxis of neurodegenerative disease.

"Prevent," "prevention," and "prophylaxis" are potent terms implying that the method of prevention, or a prophylactic agent will necessarily prevent a

neurodegenerative disease in every subject that receives the claimed method of prevention. No neurodegenerative disease will occur at any point following administration of the claimed compounds of formula (I), (II), and/or (III);

b. *Nature of the invention*: The nature of the invention is a treatment method for various Parkinson's disease and ischemia/reperfusion injury comprising administration of formulae (I), (II), or (III);

c. *The state of the prior art*: Ito, et al. (European Application EP 1 132 085, 2001, provided in IDS) teach that oxygen free radicals cause various *in vivo* reactions including ischemic disease and nervous disease accompanied by nerve degeneration (paragraph 0004). Floyd, et al. (US Patent No. 5,036,097, 1991), teach that oxygen scavengers are therapeutically effective for the treatment of ischemia/reperfusion (col 2, lines 11-15). Atlas, et al. (US Patent No. 6,420,429, 2002), teach that oxygen scavengers are therapeutically effective for the treatment of Parkinson's disease (col 4, lines 40-44).

At present, there are no known methods to prevent many neurodegenerative diseases, such as Alzheimer's or Parkinson's diseases. These diseases are generally multifactorial, and possess a dominant genetic influence. Specifically with regards to Parkinson's disease, Miller, et al. (Metabolism, 2008), teach that numerous factors are associated with the onset of Alzheimer's or Parkinson's diseases. Such influences may occur early in life and only manifest themselves at a later age.

The diseases and pathologies claimed are diverse in nature and require therapies that are neither overlapping nor obvious over each other. Treatments for cancer are not routinely utilized to treat epilepsy or hypertension;

d. *Level of one of ordinary skill in the art*: An ordinarily skilled artisan would comprise physicians and scientists investigating CNS-related disorders. The level of skill would be high;

e. *Level of predictability in the art*: There appears to be little unpredictability in the art. Many neurodegenerative diseases (i.e. Parkinson's disease) cannot be prevented. Oxygen scavengers, such as formula (I), (II), and (III) are effective treatments for Parkinson's disease and ischemia/reperfusion injury;

f. *Amount of direction provided by the inventor*: Applicant suggests that oxygen free radicals can cause a host of diseases and disorders (instant specification, pg 1), and that neutralizing the reactive oxygen species would be an effective therapeutic or prophylactic treatment for a host of diseases, including Parkinson's disease, multiple sclerosis, ischemia/reperfusion injury, and inflammation;

g. *Existence of working examples*: Applicant demonstrates in murine treatment models of Parkinson's disease and ischemia/reperfusion that the claimed compounds are therapeutically effective (Tables 1 and 2). Applicant also demonstrates that a pretreatment of rats 5 minutes prior to induction of Parkinson's disease prevented the onset of paraquat-induced seizures; and,

h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: Applicant has successfully demonstrated that formula (III) can effectively treat Parkinson's disease and ischemia/reperfusion injury. There is no more suggestion in the art to indicate that the claimed compounds would be effective therapies for all other neurodegenerative diseases or various pathologies of Claim 6 (excepting

ischemia/reperfusion). The instant specification does not make up for this deficiency. Therefore undue experimentation would be required to use the invention for the treatment of diseases other than Parkinson's disease, or pathologies related to disorders/diseases other than ischemia/reperfusion injury.

Although Applicant has demonstrated that the claimed compounds have prevented a murine-model of drug-induced Parkinson's disease, the instant specification remains not enabled for preventing any disease. The data provided by Applicant occurred in a scientific setting in which many variables, such as life style and genetic homogeneity, are controlled. The disclosure in the specification is not sufficient to overcome the teachings of Miller, et al. who disclose that both the predisposition towards Alzheimer's and Parkinson's diseases occur early in life. Applicant has not demonstrated that the claimed compound can overcome such a predisposition. Undue and unpredictable experimentation would be required to use the invention as a prophylactic therapy for Parkinson's disease, let alone all neurodegenerative diseases. Therefore the instant specification does not enable one of ordinary skill to use the invention commensurate with the scope of the rejected claims.

12. Claims 1 and 5-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the composition of formula (I) and use thereof wherein R1 and R2 are hydrogen, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, and C_2-C_{12} alkynyl, does not reasonably provide enablement for a composition of formula (I) or use thereof wherein R1 and R2 together form a tetramethylene or pentamethylene group. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The Wands factors are discussed below:

a. *The breadth of the claim*: The rejected claims are drawn to a composition of formula (I) or use thereof wherein R_1 and R_2 can independently be hydrogen, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, or C_2-C_{12} alkynyl or together can form a tetramethylene or pentamethylene group;

b. *Nature of the invention*: The nature of the invention is a composition of formula (I) or use thereof wherein R_1 and R_2 can be hydrogen, C_1-C_{12} alkyl, C_2-C_{12} alkenyl, or C_2-C_{12} alkynyl;

c. *The state of the prior art*: The composition of formula (I) is known in the prior art. Preferred embodiments include R1 and R2 as methyl groups (Paolini and Pedulli US Patent No. 5,981,548, 1999, provided in IDS);

d. *Level of one of ordinary skill in the art*: see above;

e. *Level of predictability in the art*: Oxygen scavengers, such as formula (I), (II), and (III) are effective treatments for Parkinson's disease and ischemia/reperfusion injury. Examiner found no instances of R_1 and R_2 together being a tetramethylene or pentamethylene group;

f. *Amount of direction provided by the inventor*: Applicant discloses that R_1 and R_2 can, together, be tetramethylene or pentamethylene;

g. *Existence of working examples*: Applicant provides no working examples indicating that the composition of formula (I) wherein R_1 and R_2 form a cyclic group would be effective treatments for any pathology; and,

h. *Quantity or experimentation needed to make or use the invention based on the content of the disclosure*: Applicant does not disclose how to make or use the composition of formula (I) wherein R_1 and R_2 together form a tetramethylene or pentamethylene group. The instant specification provides no guidance for one of ordinary skill in the art to make and use the invention commensurate with the scope of the rejected claims. The prior art does not make up for this deficiency, such that the instant specification is not considered enabling for the entire scope of the rejected claims.

Claim Rejections - 35 USC § 101

2. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

3. Claims 1-8 are rejected under 35 U.S.C. § 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-4 and 7-9 are rejected under 35 U.S.C. 102(b) as being anticipated by Paolini and Pedulli (above).

6. Although drawn to a nonstatutory category, Claims 1-4 are interpreted and methods of making formula (I), (II), and (III) for art purposes. Claims 2-4 limit the substituents R_1, R_2, R_3, R_4, R_5, R_6, and R_7 of formula (I). Claim 7 further limits the claimed formulae to be in a pharmaceutical or veterinary composition suitable for oral, parenteral, inhalatory or topical administration. Claim 8 further limits the claimed formulae to be in a dosage form suitable for administration in quantities of between 0.01-200 mg/kg body weight. Claims 9 and 10 are drawn to the pharmaceutical composition comprising formula (I). Claim 10 adds the limitation that R_6 and R_7 are not both hydroxyl.

7. Paolini and Pedulli teach a composition identical to formula (I) that contains identical substituents of the instant application. Moreover, Paolini and Pedulli teach the method of making formula (I) (col 4, lines 25-63). Paolini and Pedulli also teach compositions suitable for oral and parenteral administration (col 7, lines 20-30), and a single dose of 1-100 mg (col 7, lines 46-47). Although Paolini and Pedulli do not teach the dose normalized to body weight, the range taught in this prior art falls within the range of Claim 8. Therefore, Paolini and Pedulli anticipate all the limitations of the rejected claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are

> such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claim 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli (above).

10. Claim 10 of the instant application is drawn to a pharmaceutical composition of formula (I) wherein R_6 and R_7 are independently hydrogen, oxyl, or hydroxyl provided that they are not at the same time hydroxyl groups.

11. Paolini and Pedulli teach composition of formula (I) wherein both R_6 and R_7 are hydroxyl. However, it is known that the oxygen of an hydroxyl group, when in solution, can lose the hydrogen to become an oxyl group. Therefore, the composition of Claim 10 is a *prima facie* obvious variant of the composition taught by Paolini and Pedulli.

12. Claims 5 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Paolini and Pedulli as applied to claim 10 above, and further in view of Ito, et al. (above), Floyd, et al., (above), and Atlas, et al. (above)

13. Claims 5 and 6 of the instant application are drawn to a method of treating various neurodegenerative diseases (i.e. Parkinson's or Alzheimer's diseases) comprising using (e.g. administrating) formula (I).

14. Paolini and Pedulli teach formula (I), and that formula (I) is a superoxide scavenger. Paolini and Pedulli do not teach a method of treating a disease with formula (I).

15. Ito, et al. teach that oxygen free radicals cause various *in vivo* reactions including ischemic disease and nervous disease accompanied by nerve degeneration (paragraph 0004). Floyd, et al., teach that oxygen scavengers are therapeutically effective for the treatment of

ischemia/reperfusion (col 2, lines 11-15). Atlas, et al., teach that oxygen scavengers are therapeutically effective for the treatment of Parkinson's disease (col 4, lines 40-44).

Conclusion

16. Claims 1-10 are rejected.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul Zarek whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Rita J. Desai/
Primary Examiner, Art Unit 1625